EMORD & ASSOCIATES, P.C.

BURKE PROFESSIONAL CENTER
5282 LYNGATE COURT
BURKE, VIRGINIA 22015

—

1050 SEVENTEENTH STREET, N.W.
SUITE 600
WASHINGTON, DC 20036

—

PHONE: (202) 466-6937 • FAX: (202) 466-6938
WEB SITE: www.emord.com
E-MAIL: jemord@emord.com

August 15, 2002

VIA FACSIMILE (without attachments) *301-827-3054*
AND VIA HAND
Daniel Troy
Chief Counsel
Food and Drug Administration
Room 657 (GCF-1)
5600 Fishers Lane
Rockville, MD 20857

Re: Dr. Kyl Smith's Health Claim Petition for Phosphatidylserine

Dear Dan:

This letter follows our correspondence of July 15, 2002 and our telephone discussion earlier that same day concerning the above-referenced petition. In our discussion you explained that the agency questions whether phosphatidylserine is a new dietary ingredient. You asked Dr. Smith to make a submission on that point. This letter and the documents appended to it are that submission.

A dietary supplement is deemed adulterated under 21 U.S.C. § 342(f) if it contains a "new dietary ingredient" unless that ingredient (1) has been "present in the food supply as an article used for food in a form in which the food has not been chemically altered" or (2) has "a history of use or other evidence of safety . . . that the dietary ingredient when used under the conditions recommended or suggested in . . . labeling . . . will reasonably be expected to be safe." 21 U.S.C. § 350b(a). Under 21 U.S.C. § 350b(c), a "new dietary ingredient" is "a dietary ingredient that was not marketed in the United States before October 15, 1994 and does not include any dietary ingredient which was marketed in the United States before October 15, 1994."

Phosphatidylserine Is Not a New Dietary Ingredient. Lucas Meyer, Inc., (a company acquired by Degussa Health & Nutrition Americas, Inc. in November 2001 (Degussa)), began marketing a soy-based phosphatidylserine dietary supplement, LECI-PS, in daily dose amounts ranging from 100 mg to 300 mg on August 1, 1994. Degussa continues to market LECI-PS to this day. See www.degussa-bioactives.com/bioactives/html/e/

02P.0413

SUP1

products/overview/europe/phospholipids/pdylserine.htm. Evidence of that marketing consists of: (1) the Lucas-Meyer "LECI-PS" trademark file acquired by this firm from the United States Patent and Trademark Office (Exhibit 1); (2) affidavits and attachments from former Lucas Meyer Vice President Scott Hagerman (Exhibits 2 and 3); and a Lucas Meyer invoice (Exhibit 4). In addition, the Life Extension Foundation of Hollywood, Florida began marketing a phosphatidylserine dietary supplement, COGNITIX, in July 1988, and continues to do so to the present. Exhibits 5;6. Evidence of that marketing consists of: (1) an affidavit and attachments from Life Extension Foundation Call Center Manager Francine DiDonato (Exhibit 5) and (2) an affidavit from Life Extension Foundation Web Editor Dayna Dye (Exhibit 6).

The Lucas-Meyer LECI-PS trademark file includes a sworn statement from that company's president, Peter Rohde, that Lucas Meyer, Inc. "first used the mark [LECI-PS] on or in connection with the above-identified goods"[1] and "in interstate commerce" "at least as early as August 1, 1994 . . ." Exhibit 1. The file includes a copy of the label containing the mark first used in commerce. That label identifies the contents of the dietary supplement as "high phosphatidylserine soy lecithin." On the principal display panel beneath the product name appears "PS-enriched soy lecithin." Exhibit 1. Exhibit 4 is a Lucas Meyer invoice, dated August 1, 1994, showing a $5 order and shipment on that same date of 1 bottle of LECI-PS to Valentine Industries, 940 Collins Hill Road, Lawrenceville, GA 30243. Exhibit 4.

The affidavit attached as Exhibit 2 includes the sworn statement of Scott Hagerman, Vice President of Lucas Meyer, Inc. from November 1993 until May 1999. Mr. Hagerman states: "Company records . . . confirm that the first use of the mark [LECI-PS] in interstate commerce occurred on August 1, 1994, at which time LECI-PS was sold to Valentine Enterprises of Lawrenceville, Georgia." Mr. Hagerman goes on to state that he is aware that an Israeli company, Lipogen of Haifa, Israel, "marketed phosphatidylserine to Americans for use as a dietary supplement before October of 1994." He states that "in the summer of 1994, I had in my Lucas Meyer office in Decatur, Illinois Lipogen's phosphatidylserine dietary supplement L-TELLECT which I acquired from that company by purchase earlier in the year." Exhibit 2.

The affidavit attached as Exhibit 3 includes another sworn statement of Scott Hagerman. In that statement Hagerman explains that LECI-PS at the time it was sold to Valentine Enterprises, Inc. had a serving size containing 100 mg of phosphatidylserine and a daily use range from one to three servings per day. Exhibit 3. He also supplies a sales brochure for LECI-PS by Lucas Meyer, Inc. to Rexall Sundown on September 1, 1994. Exhibit 3.

The affidavit attached as Exhibit 5 is the sworn statement of Francine DiDonato. In that sworn statement, Ms. DiDonato states that she was employed as a sales clerk at the Life Extension Foundation in Hollywood, Florida from September 1983 until approximately 1996. She states that Life Extension Foundation began marketing a

[1] The application includes label copy bearing the title, "LECI-PS (PS-enriched soy lecithin)," and the content description, "high phosphatidylserine soy lecithin."

dietary supplement containing 100 mg of phosphatidylserine per capsule, COGNITIX, in July of 1988. Exhibit 5. She further states that Life Extension Foundation records show sales of 5,890 bottles of COGNITIX between October 29, 1993 and October 15, 1994. Exhibit 5.

The affidavit attached as Exhibit 6 is the sworn statement of Dayna Dye. Ms. Dye states that she took COGNITIX as a dietary supplement intermittently from 1988 until 1994. Exhibit 6.

Based on the foregoing evidence, Dr. Kyl Smith concludes that phosphatidylserine is not a new dietary ingredient. It has been marketed in the United States as a dietary supplement before October 15, 1994, and, thus, does not fall within the statutory definition in 21 U.S.C. § 350b(c).

Phosphatidylserine Has Been Present in the Food Supply as an Article Used for Food in a Form in which the Food Has Not Been Chemically Altered.
American cuisine has included cow and pig brains containing high levels (809 mg to 1046 mg) of phosphatidylserine per serving since at least the early part of the twentieth century. See Exhibit 7: The Boston Cooking-School Cook Book by Fannie Farmer (1918) (http://www.bartleby.com/87/), Chapter XII, para. 19 ("Other Parts of Beef Creature Used for Food"); Chapter XXII, para. 26 ("Calf's Brains Fritters"); and Chapter XXXV, para. 8 ("Scrambled Eggs with Calf's Brains"); Saint Louis Today (2/12/2002) http://www.stltoday.com/stltoday/entertainment/columns.nsf/Local%20Flavor/1C5D2807F72249, "Local Flavor: Brain, the other white meat;" and Bobowick, A. et al., Cruetzfeldt-Jakob Disease: A Case-Control Study, American J. of Epidemiology, Vol 8, N. 5, 381, 390 (1973). One publication dated 1997 quotes USDA sources as estimating that approximately one million animal brains are removed for human consumption each year. Exhibit 8 at 8.

"Bovine and porcine cerebral phospholipids naturally contain phosphatidylserine (PS) in the same amount and fatty acid composition as found in the human brain." Exhibit 9 at 47[2]; see also reference number 278 to Dr. Glade's scientific report appended to Dr. Smith's Health Claim Petition. Phosphatidylserine is present in high quantitative amounts in the brains of pigs and cows. See Exhibit 10 at 1 (715.8 mg to 925.5 mg of phosphatidylserine are present in every 100g of either raw cow brain or raw pig brain).[3] It is thus the case that Americans since at least the first decade of the twentieth century

[2] Phosphatidylserine is 10.06% of the total lipid content of the grey matter and 7.78% of the total lipid content of the white matter of the human brain. Exhibit 9.

[3] Those figures were calculated by applying the percentage of phosphatidylserine in human brain white and grey matter to the total lipid content of raw cow and pig brain. Exhibit 9 shows those calculations step by step and citations supporting those equations. The total lipid content of 100g of raw cow brain and raw pig brain are within 6/100ths of each other. Raw cow brain is 9.21g total lipids per 100g of raw brain. Raw pig brain is 9.28g total lipids per 100g of raw brain. U.S. Department of Agriculture, Agricultural Research Service. 2001. USDA Nutrient Database for Standard Reference, Release 14. Nutrient Data Laboratory Home Page, http://www.nal.usda.gov/fnic/foodcomp; (hereinafter USDA Nutrient Database"), NDB No. 13318 "Beef, variety meats and by-products, brain, raw." The calculation was made for 9.2 grams per 100g of raw brain and is thus applicable to both cow and pig brain content.

have consumed phosphatidylserine in foods at levels equal to or exceeding 808.854 mg to 1045.815 mg per every 113 gram serving.[4]

Phosphatidylserine is a structural component of the cell membranes of all animals, plants, and other life forms. Exhibit 11. It is thus present in every food derived from plants and animals, including the ubiquitous commercial lecithin—a common dietary ingredient in a wide variety of foods, including vegetable oil, whole grain cereals and whole grain baked goods, egg yolks, liver, and milk. See,e.g., www/nutrition4health.org/ NOHAnews/NNSp01_Lecithin.html; www.greenline.com/health/lecithin.shtml; www.preparedfoods.com/archives/1998/9811fats.htm; PDR for Nutritional Supplementsat 351-354.[5]

Based on the foregoing evidence, Dr. Kyl Smith concludes that even were phosphatidylserine a new dietary ingredient, it could not be deemed adulterated under 21 U.S.C. § 350b(a)(1) because it has been present in the food supply as an article used for food in a form in which the food has not been chemically altered since at least the first decade of the twentieth century. Moreover, the decades long consumption of even high quantitative amounts of phosphatidylserine in pig and cow brains without significant adverse effects attendant to phosphatidylserine ingestion leads ineluctably to the conclusion that phosophatidylserine is a safe dietary ingredient. The scientific report of Michael John Glade, Ph.D., F.A.C.N. appended to Dr. Smith's Health Claim Petition reviews substantial additional safety evidence on phopsphatidylserine and concludes, conservatively, that it is without any significant adverse effects at dose levels up to 500 mg per day. See Dr. Glade's scientific report appended to Dr. Smith's Health Claim Petition, Exhibit 1 at 8-9.

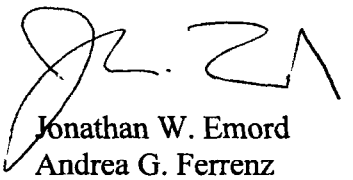
For the foregoing reasons, we respectfully request that the agency find phosphatidylserine not a new dietary ingredient because it was marketed as a dietary supplement in the United States before October 15, 1994. Moreover, even were it erroneously declared a new dietary ingredient, it should not be deemed adulterated because it fits within the exception in 21 U.S.C. § 350b(a)(1), to wit: It has been present in the food supply as an article used for food in a form in which the food has not been

[4] A typical serving size of a meat dish is 4 oz. 4 ounces equals 113.00 grams. USDA Nutrient Database NDB No. 13318 "Beef, variety meats and by-products, brain, raw."

[5] The PDR explains, "[c]hemically, lecithin is phosphatidylcholine. Commercially, it refers to a natural mixture of neutral and polar lipids." PDR for Nutritional Supplements at 351; 354.

chemically altered. Finally, its mass consumption as a food for at least nine decades and the aforementioned scientific evidence in Dr. Glade's report establish a history of safe use sufficient to satisfy the exception contained in 21 U.S.C. § 350b(a)(2).

Sincerely,



Jonathan W. Emord
Andrea G. Ferrenz
Jonathan A. Goodman

Attachments
cc: Dr. Kyl Smith